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## NOTICE OF ALLOWANCE AND FEE(S) DUE

10117 7590 10/08/2008

ZYMOGENETICS, INC.  
INTELLECTUAL PROPERTY DEPARTMENT  
1201 EASTLAKE AVENUE EAST  
SEATTLE, WA 98102-3702

EXAMINER

JIANG, DONG

ART UNIT

PAPER NUMBER

1646

DATE MAILED: 10/08/2008

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/664,432

09/19/2003

Charles E. Hart

00-12D1

5728

TITLE OF INVENTION: METHODS FOR PROMOTING GROWTH OF BONE, LIGAMENT, AND CARTILAGE

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	YES	\$755	\$300	\$0	\$1055	01/08/2009

**THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.**

**THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.**

### HOW TO REPLY TO THIS NOTICE:

#### I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status above is to be removed, check box 5b on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

**IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.**

# **PART B - FEE(S) TRANSMITTAL**

**Complete and send this form, together with applicable fee(s), to: Mail Mail Stop ISSUE FEE  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
or Fax (571)-273-2885**

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

10117 7590 10/08/2008

**ZYMOGENETICS, INC.**  
**INTELLECTUAL PROPERTY DEPARTMENT**  
**1201 EASTLAKE AVENUE EAST**  
**SEATTLE, WA 98102-3702**

## **Certificate of Mailing or Transmission**

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/664,432 09/19/2003 Charles E. Hart 00-12D1 5728

TITLE OF INVENTION: METHODS FOR PROMOTING GROWTH OF BONE, LIGAMENT, AND CARTILAGE

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
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nonprovisional YES \$755 \$300 \$0 \$1055 01/08/2009

EXAMINER	ART UNIT	CLASS-SUBCLASS
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JIANG, DONG 1646 424-085100

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.

☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

(1) the names of up to 3 registered patent attorneys or agents OR, alternatively, 1 \_\_\_\_\_

(2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed. 2 \_\_\_\_\_

3 \_\_\_\_\_

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

(B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ☐ Individual ☐ Corporation or other private group entity ☐ Government

4a. The following fee(s) are submitted:

- ☐ Issue Fee  
☐ Publication Fee (No small entity discount permitted)  
☐ Advance Order - # of Copies \_\_\_\_\_

4b. Payment of Fee(s); (Please first reapply any previously paid issue fee shown above)

- ☐ A check is enclosed.  
☐ Payment by credit card. Form PTO-2038 is attached.  
☐ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number \_\_\_\_\_ (enclose an extra copy of this form).

5. Change in Entity Status (from status indicated above)

- ☐ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27. ☐ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature \_\_\_\_\_

Date \_\_\_\_\_

Typed or printed name \_\_\_\_\_

Registration No. \_\_\_\_\_

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

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ZYMOGENETICS, INC.  
INTELLECTUAL PROPERTY DEPARTMENT  
1201 EASTLAKE AVENUE EAST  
SEATTLE, WA 98102-3702

## Determination of Patent Term Adjustment under 35 U.S.C. 154 (b) (application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 511 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 511 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (<http://pair.uspto.gov>).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

<b>Notice of Allowability</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/664,432	HART ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	DONG JIANG	1646	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--**

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to the response filed on 7/2/08.
2. ☒ The allowed claim(s) is/are 2-9, 11 and 22-25 to issue as claims 2-4, 6, 8, 5, 9, 7, 1 and 10-13.
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) ☐ All    b) ☐ Some\*    c) ☐ None    of the:
    1. ☐ Certified copies of the priority documents have been received.
    2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
    3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\* Certified copies not received: \_\_\_\_.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

**THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS ( as "replacement sheets") must be submitted.
  - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review ( PTO-948) attached
    - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date \_\_\_\_.
  - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date \_\_\_\_.

**Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).**
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

**Attachment(s)**

- |  |   |
|--|---|
| 1. <input type="checkbox"/> Notice of References Cited (PTO-892)   | 5. <input type="checkbox"/> Notice of Informal Patent Application                     |
| 2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 6. <input type="checkbox"/> Interview Summary (PTO-413),<br>Paper No./Mail Date ____. |
| 3. <input type="checkbox"/> Information Disclosure Statements (PTO/SB/08),<br>Paper No./Mail Date ____     | 7. <input type="checkbox"/> Examiner's Amendment/Comment                              |
| 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit<br>of Biological Material | 8. <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance  |
|  | 9. <input type="checkbox"/> Other ____.   |

### **DETAILED OFFICE ACTION**

The request filed on 02 July 2008 for a Continued Examination (RCE) under 37 CFR 1.114 based on parent Application No. 10/664,432 is acceptable, and a RCE has been established. An action on the RCE follows.

Applicant's response filed on 02 July 2008 is acknowledged and entered.

Currently, claims 2-9, 11 and 22-25 are pending and under consideration.

#### **Withdrawal of Objections and Rejections:**

All prior art rejections of claims 2-9, 11 and 22-25 made in the last Office Action are withdrawn for the reasons below.

#### **Examiner's Statement of Reasons for Allowance**

The following is an examiner's statement of reasons for allowance: claims 2-9, 11 and 22-25 of the present invention are directed to a method for promoting growth of bone, ligament, or cartilage by administering a composition comprising a homodimer protein, wherein each of the polypeptide chains consists of residues X-345 of SEQ ID NO:2, and X is an integer from 226 to 235, inclusive. The polypeptide of SEQ ID NO:2 is believed to be a member of VEGF family, and designated zveg3. Prior art search results reveal that Ferrara et al. (US6,455,283 B1) discloses a human vascular endothelial growth factor, VEGF-E, which amino acid sequence of SEQ ID NO:2 is 100% identical to the present SEQ ID NO:2, and can form hetero- and homodimers. Additionally, Ferrara teaches that VEGFE may be used to stimulate wound healing or tissue regeneration and associated therapies connected with regrowth of tissues such as, among others, connective tissue, skin, bone, cartilage, and would be useful for indications where angiogenesis is desired such as, among others, osteoporosis, and has application in the healing of bone fractures and cartilage damage or defect in humans or other animals. Ferrara does not specifically teach the function growth factor domain of VEGF-E, consisting of residues X-345, wherein X is an integer from 226-235 comprising, nor the homodimer thereof, as that in the instant invention.

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The examiner rejected the present claims based on the Ferrara reference, indicating that it would have been obvious to make the homodimer of the polypeptide fragments as defined in the instant claims because mapping out a functional fragment or defining the structural-functional relationship of a newly discovered protein was both desirable and routine in the art at the time the present invention was filed, so long as the sequence and functional activity were known. For supporting evidence, the examiner cited Uutela et al. (US7,105,481), which discloses a new member of the PDGF/VEGF family of growth factors, PDGF-D, which is closely related to the PDGF-C in the instant application, and stimulates connective tissue growth or wound healing. Additionally, Uutela teaches that an additional member of the PDGF/VEGF family, PDGF-C, has a two-domain structure, a N-terminal CUB domain, and a C-terminal PDGF/VEGF homology domain, and PDGF-C requires proteolytic removal of the N-terminal CUB domain for receptor binding and activation of the receptor. Further, Uutela teaches that PDGF-D also comprises a N-terminal CUB domain, and a C-terminal PDGF/VEGF homology domain, and teaches a truncated form of PDGF-D with N-terminal truncation, and comprising residues 254-370 of SEQ ID NO:8 (a portion of the PDGF/VEGF homology domain of PDGF-D), which extends toward the N-terminus up to residue 234 of SEQ ID NO:8 (column 8, lines 24-36), and that the truncated homodimer PDGF-DD retains the functional activity.

Applicants argue, in the response filed on 02 July 2008, 1) that the Uutela reference is not prior art to the instant application, as only one of its U.S. provisional application, 60/107,852, was filed prior to Applicants' effective filing date of December 7, 1998, and it does not disclose a two domain structure for either PDGF-C or PDGF-D, and does not teach or suggest a "truncated form of PDGF-D comprising residues 254-370 of SEQ ID NO:8 (pages 5-6); 2) that the inventive entity of the Uutela patent, including the claimed priority applications, includes Dr. Ulf Eriksson, whose research has been particularly focused on the PDGF/VEGF family of growth factors, including PDGF-C and PDGF-D, accordingly, Dr. Eriksson is a person of particularly high expertise with regard to PDGF/VEGF growth factor family members, including PDGF-C and -D, and the Uutela reference cannot be considered as representative of an ordinarily skilled artisan, and thus the scientific work discussed in Uutela relating to PDGF-C and -D cannot be presumed *a priori* to have been "routine" in the art (pages 6-7).

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While applicants argument regarding point 2) is not sound, the first point (point 1)) is persuasive: although the Uutela reference is not used for the prior art rejection per se, the fact that the relevant content of Uutela was disclosed after Applicants' effective filing date does not suggest that the "routine" indicated by the examiner had been established in the art at the time of the present invention was filed. As such, the prior art rejections are withdrawn.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

**Conclusion:**

Claims 2-9, 11 and 22-25 are allowed.

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**Advisory Information:**

Any inquiry concerning this communication should be directed to Examiner Dong Jiang whose telephone number is 571-272-0872. The examiner can normally be reached on Monday - Friday from 9:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Dong Jiang/, Ph.D.  
Primary Examiner, Art Unit 1646  
9/18/08

Application/Control Number: 10/664,432

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